UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,150	12/15/2003	Frank E. Blondino	033018-121	2098

21839 7590 12/27/2006

BUCHANAN, INGERSOLL & ROONEY PC
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,150	BLONDINO ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-14,18 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17,19 and 23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/04, 06/04, 11/04, 06/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 18, 20-22 are withdrawn from further consideration as being drawn to a non-elected species. Applicant timely **traversed** the restriction (election) requirement in the reply filed on 11/27/06. No arguments for the traversal have been cited by Applicant. Accordingly, claims 15-17, 19 and 23-30 are under examination at this time.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17, 19 and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite for failing to further limit the parent claim. The parent claim 15 already recites a method, wherein the liquid formulation includes "at least one thermally stable active ingredient". Claim 17 recites that the formulation "further" includes at least one thermally stable active ingredient, however there is already one active agent claimed.

Claim 19 is also indefinite for failing to further limit the parent claim. The parent claim 17 already recites particles "having an MMAD of less than 3 micron".

Claim 26 is vague for reciting the term "derivatives thereof". The specification does not adequately recite derivatives of active agents such as buprenorphine.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15-17, 19, 23-24, 26-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Rabinowitz et al (US20040202617).

Rabinowitz et al teach delivery of opioids through an inhalation route. Specifically, an aerosol containing opioids that are used in inhalation therapy is disclosed. Also a method of delivery is disclosed which method comprises heating a thin layer of an opioid, on a solid support, to from a vapor, and passing air through the heated vapor to produce aerosol particles having less than 5% opioid degradation products (see abstract).

It is disclosed that typically, the aerosol particles have a mass median aerodynamic diameter (MMAD) of less than 5 microns. Preferably the particles have an MMAD of less than 3, less than 2 or less than 1 micron (see [0013], [0043] and [0054]).

Suitable active agents for the said aerosol vapor formulation include buprenorphine or its salts (see [0015], [0017], [0023], [0097], [0171] and [0172]). The formulations may contain one or more excipients such as propylene glycol, glycerol, ethanol, methanol, etc (see [0140] and [0143]).

One device used to make and deliver the said opioid containing aerosol has a proximal end, a distal end, a heating module, a power source and a mouthpiece. An opioid composition is deposited on a surface of heating module. Upon activation of a user activated switch power source initiates heating of heating module through ignition of combustible fuel or passage of current through resistive heating element. The opioid composition volatizes due to the heating of heating module and condenses to form a condensation aerosol prior to reaching the mouthpiece at the proximal end of the device (see [0145] and [0148]). Examples 3 and 4 disclose a method of producing inhalable particles of buprenorphine aerosol.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15, 17, 19, 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hodges et al (6,682,716).

Hodges et al teaches inhalation delivery of aerosols containing small particles. Specifically, delivery of drug containing aerosols having particles with a mass median aerodynamic diameter (MMAD) of less than 1 micron for inhalation therapy (see abstract).

Suitable drugs for the said aerosol formulations include buprenorphine, busprione, zolpidem, etc or a mixture thereof (see col. 6, lines 15-42; col. 8, lines 27-28 and 40-44). The aerosolization device is operably connected to the flow meter. A dose of the compound is deposited onto thin, stainless steel foil. In most cases, compound is deposited by making a solution of the compound with an organic solvent (col. 9, lines 24-26, 51-56). The said foil functions as both a substrate for the drug to be delivered to the subject and the heating element for the vaporization of the drug. Heating element is heated primarily by eddy currents induced by an alternating magnetic field. The device also comprises a lower airway section which is mounted on top of chassis that houses the electronics, magnetic field generator, stepper motor and position sensors. Mounted

in airway section is upstream passage and inlet orifice that couples upper airway section to flow meter. The readings from the flow meter are fed to the electronics housed in chassis. Additionally, at the downstream end of airway passage, outlet is connected to mouthpiece (col. 10, line 29 to col. 11, line 1).

Hodges et al also disclose in Example 900 that the internal resistance of the screen was from 0.01 to 0.2 ohms and that the discharge rate of the capacitor was rapid.

Although Hodges et al does not exemplify a method of generating a vapor formulation comprising buprenprphine or a salt thereof, it would have been obvious to one of ordinary skill in the art to have prepared a vapor formulation for aerosolized delivery of buprenorphine and other medicaments, because Hodges et al provide sufficient disclosure to one of ordinary skill in the art to make and use the invention as claimed. Specifically, Hodges et al teach a method of making and delivering vapor aerosols of medicaments to patient's pulmonary system, and disclose that said formulations have a high purity rate and are delivered to the site faster than other methods of delivery. Hodges also discloses the device and the steps of making the said vapor formulations.

Claims 15, 17, 19, 23-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al (7,040,314).

Nguyen et al teaches a liquid aerosol formulations for generating aerosols include at least one high volatility carrier and a second component. An aerosol generating device generates an aerosol by passing liquid aerosol formulation through a flow passage heated to convert the liquid into a vapor, which is mixed with air to form an aerosol. In some embodiments, particles of the aerosol consist essentially of the second component. The aerosol generator can be delivered to a targeted portion of the lung using the inhaler (see abstract). One of the suitable classes of medicaments for the said aerosol formulation is opioids and a suitable species is buprenorphine (see col. 7, lines 9-13). The said liquid aerosol formulation is flowed through a capillary-sized flow passage in which the liquid is heated to a sufficiently high temperature to vaporize the liquid.

Nguyen et al also discloses that the liquid source includes an upstream flow passage that provides fluid communication from the reservoir to the flow passage. The aerosol generating device preferably includes at least one valve disposed to control flow of the liquid source into the heater unit (col. 9, lines 52-67). As the fluid flows through the capillary passage into the heated region between the first and second electrodes, the fluid is heated and converted to a vapor. The vapor passes from the heated region to a vapor. The volatized fluid is entrained in ambient air as the volatized fluid exits from the outlet, causing the volatized fluid to form an aerosol such as a condensation aerosol. In a preferred embodiment, the MMAD of the aerosol particle size is about 0.5 to 2.5 micron (col. 11, lines 45-67). The resistance target is selected to correspond to a temperature that is sufficient to cause heat transfer to the liquid such that liquid is

volatized and expands out the open end of the capillary passage. The control electronics activates the heating, such as by applying for a duration of time pulsed energy to the heater (col. 12, lines 10-15). Figure 12 shows a range of from 0.21 to 0.235 ohm resistance target.

Although Nguyen et al does not exemplify a method of generating a vapor formulation comprising buprenorphine or a salt thereof, it would have been obvious to one of ordinary skill in the art to have prepared a vapor formulation for aerosolized delivery of buprenorphine and other medicaments, because Nguyen et al provides sufficient disclosure to one of ordinary skill in the art to make and use the invention as claimed. Specifically, Nguyen et al teaches a method of making and delivering vapor aerosols of medicaments to patient's pulmonary system, and discloses that said formulations have a high purity rate where the recovery rate of the active agent can be 100% with no observable degradation and sufficiently small particle sizes for inhalation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-17, 19, 23-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-18, 24-32 of copending Application No. 10/958,329 (US 20050079137). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims would have been obvious over the reference claims. Here, both the instant claims and the reference claims are drawn to a method of generating an aerosol comprising supplying a liquid aerosol formulation to a flow passage and heating the liquid to form a vapor. The active agents suitable for the said method are "a thermally stable active agent". The difference between the two applications is that in the instant claims, the active agent is buprenorphine while in the reference claims the active agent is scopolamine. It is considered that the method of generating vapors would be applicable to any "thermally stable active agent" and that substituting one agent for the other would have been obvious to one of ordinary skill in that art. It is also considered that the various "thermally stable active agents" are obvious variations of each other and substituting one for another does not alter the scope of claims. This was also apparent from the election of species requirement.

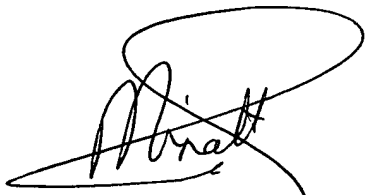
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Byron et al (US 20040016427) teaches methods and apparatus for generating an aerosol. An aerosol is formed by supplying a material in liquid form to a flow passage and heating the flow passage such that the material volatizes and expands out of an open end of the flow passage. Byron lacks disclosure on buprenorphine or a salt thereof.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mina Haghighatian
Patent Examiner
Art Unit 1616
December 15, 2006